

Common Carp Pituitary Clinical Field Trials - INAD 8391

Year 2004 Annual Summary Report on the Use of Common Carp Pituitary in Field Efficacy Trials

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Summary

Spawning aids such as common carp pituitary (CCP), luteinizing hormone-releasing hormone analogue, and human chorionic gonadotropin are routinely used in fisheries programs to induce gamete maturation in fish to enhance fish propagation programs. The U.S. Food and Drug Administration has authorized the use of CCP under the Compassionate Investigational New Animal Drug (INAD) Exemption #8391 for the purpose of gathering efficacy data to support a new animal drug approval for CCP. During calendar year 2004 (CY04), several INAD trials were conducted to evaluate the efficacy of CCP to induce gamete maturation in a variety of fish species. Thirty-six such trials that involved 1,698 treated fish were conducted at four different fish hatcheries, including one U.S. Fish and Wildlife Service fish hatchery, two state hatcheries, and one private hatchery. Efficacy was determined by whether or not treated fish (1) produced or yielded eggs or milt, or (2) produced or yielded more eggs or milt than untreated fish. Overall results of trials conducted in CY04 indicated that approximately 81% of the trials

appeared efficacious, 3% of the trials appeared ineffective, and 16% of the trials were characterized as inconclusive.

Introduction

The use of hormones to induce spawning in fish is critical to the success of many federal, state, private, and tribal fisheries programs. A wide variety of programs, including several that involve the restoration of threatened/endangered species are dependent upon hormone treatment to complete final gamete maturation and ensure successful spawning.

The time of spawning is by its own nature a stressful period for all fish species. The handling required during the artificial spawning of fish complicates an already delicate situation. In order to maintain the health of both wild and domestic brood fish, it is beneficial to minimize overall fish handling. Successful hormone treatment can reduce handling requirements to a single hormone administration event followed by actual gamete collection, thereby greatly reducing overall fish handling. In many cases, especially with respect to captured wildstock species, final gamete maturation will not occur without hormone treatment.

Final gamete maturation in fish can be induced by the administration of various spawning hormones. Common carp pituitary (CCP) is one such hormone, and has been shown to induce gamete maturation in a number of fish species, including certain

threatened and endangered species. Common carp pituitary, which has been shown to be particularly effective when used in cool and warm water species, has had a significant, positive impact on federal, state, private, and tribal programs nationwide.

Purpose

The purpose of this report is to summarize the results of CY04 supplemental CCP field efficacy trials. Furthermore, it is expected that these data will be used to enhance the existing CCP database that has been established from previous years trials for the purpose of supporting a new animal drug approval for the use of CCP in aquaculture.

Facilities, Materials, and Methods

1. Participating Facilities

Four fish culture facilities used CCP during CY04, including one U.S. Fish and Wildlife Service fish hatchery, two state fish hatcheries, and one private fish hatchery. Water temperature during treatments at the various testing facilities ranged from 48.0 - 78.8 °F. Overall mean treatment temperature from all trials was 72.8 °F.

2. CCP used in trials

All CCP used in CY04 trials was supplied by Stoller Fisheries, Spirit Lake, IA.

3. Drug dosages

As described in the Study Protocol, Investigators were allowed to use CCP at dosages ranging from 4 to 10 mg CCP/kg body weight (bw). The drug dosages used in these trials ranged from 2.2 to 10 mg CCP/kg bw and were used to induce gamete maturation in females and males. CCP was administered as either a single intraperitoneal (IP) injection, or as a series of two IP injections.

Fish Species and Gender Treated

1. Species of fish treated

The following three fish species were treated with CCP during the reporting period:

channel catfish *Ictalurus punctatus*

muskellunge *Esox masquinongy*

northern pike *Esox lucius*

2. Gender of fish treated

A total of 1,690 females and 8 males were injected with CCP during the reporting period. Typically, females are treated with spawning hormones to shorten the

egg maturation period or synchronize ovulation. Males are treated to ensure that sufficient milt is available for egg fertilization.

Data Collected

1. Pathologists Reports

Although fish health pathology reports provide essential information with respect to disease confirmation and general fish health, no pathology report were submitted during CY04 trials.

2. Primary response variables

The primary response variables for evaluating the effect of CCP were (1) the relative number of female fish that ovulated following treatment, or (2) the number of male fish that reached active spermiation following treatment. With respect to the treatment of females, in some cases, percent hatch and percent eyed eggs were also determined.

3. Spawning interval

The spawning interval is the period of time between the final CCP treatment and when treated fish were evaluated for gamete maturation. Where appropriate, the spawning interval was documented.

Discussion of Study Results

1. Summary results on the efficacy of CCP to induce gamete maturation (Note:

Summary of CY04 CCP efficacy results are listed in Table 1; Table 2 describes the number of trials conducted, fish species and number of fish treated, and treatment regimens used; and Table 3 describes individual CCP trials conducted at all federal, state, and private hatcheries under this INAD)

A. Efficacy at 2.2 mg/kg bw

One trial was conducted in which male muskellunge were injected with CCP at a dosage of 2.2 mg/kg bw (Table 1). Following treatment, there was 100% spermiation among all treated fish; no control fish were used. This treatment appeared efficacious.

B. Efficacy at 6.6 mg/kg bw

Six trials were conducted in which female muskellunge were injected with CCP at a dosage of 6.6 mg/kg bw (Table 1). One trial involved the use of a non-treated control group. Following treatment, there was 86% ovulation among treated females used in this trial. The control fish did not ovulate. In the trials in which controls were not used, the relative level of ovulation ranged from 0% and 100%. Overall, treatment appeared

efficacious in five of six trials, whereas results from one trial indicated treatment was not effective.

C. Efficacy at 10.0 mg/kg bw

Twenty-eight trials were conducted in which female channel catfish were injected with CCP at a dosage of 10.0 mg/kg bw (Table 1). Following treatment, the relative level of ovulation in treated channel catfish ranged from 29 to 100%. One trial was conducted in which female northern pike were injected with CCP at a dosage of 10.0 mg/kg bw (Table 1).

Following treatment, there was ovulation in 62% of the treated fish.

Among the control fish, only 20% of the fish ovulated. Overall, treatment appeared efficacious in 23 of the 29 trials, whereas six trials were characterized as inconclusive.

2. Observed Toxicity

No toxicity or adverse effects relating to CCP treatment were reported.

Summary of Study Results

The efficacy of CCP was tested in 36 trials involving muskellunge, northern pike, and channel catfish treated at dosages ranging from 2.2 to 10.0 mg/kg bw. Treatment was administered as either a single IP injection or as a series of two IP injections. Of the 36 trials conducted, two utilized non-treated control groups. A total of 1,698 adult fish were

treated (1,690 females and 8 males). Water temperature during treatment ranged from 48.0 to 72.8°F. Overall, results showed that CCP treatment appeared efficacious in 81% of the trials, ineffective in 3% of the trials, and inconclusive in the remaining 16% of the trials. Investigators reported no evidence of toxicity or adverse effects related to CCP treatment. Because of the lack of pivotal field efficacy trials, it is understood that data summarized in this report can only be considered as ancillary data. None-the-less, the ancillary data described above should provide useful corroborative data to support a new animal drug approval for CCP. It is anticipated that additional ancillary efficacy data will continue to be collected under INAD #8391. In future trials conducted under INAD #8391, efforts will be directed towards the continued generation of high quality data.

Table 1. Summary of CY04 CCP Efficacy Results							Females				Males			
							Treated		Control		Treated		Control	
Apparent Efficacy	Number of Trials	Facility	Species	Treatment Method	Dose (mg/kg)	Spawning Interval (hr)	Number Treated	% Ovulate	Number Controls	% Ovulate	Number Treated	% Spermiat	Number Controls	% Spermiat
Efficacious	22	Harvest Select Farms	Channel Catfish	Injection	10.0	26	1,394	51 - 100	0	na	0	na	0	na
Inconclusive	6	Harvest Select Farms	Channel Catfish	Injection	10.0	26	263	25 - 48	0	na	0	na	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	2.2	4 - 18 days	0	na	0	na	8	100	0	na
Efficacious	1	Table Rock SFH	Musky	Injection	6.6	4 - 18 days	8	100	0	na	0	na	0	na
Efficacious	4	Hackettstown SFH	Musky	Injection	6.6	3 - 5 days	11	86 - 100	1	0	0	na	0	na
Ineffective	1	Hackettstown SFH	Musky	Injection	6.6	-	1	0	0	na	0	na	0	na
Efficacious	1	Genoa NFH	Northern Pike	Injection	10.0	1 - 4 days	13	62	5	20	0	na	0	na

Table 2. Description of number of trials conducted, species and number of fish treated, and treatment regimens used in CY04 under INAD #8391

Total Number of Trials Conducted:	36
<u>Number of Efficacious Trials:</u>	29
<u>Number of Ineffective Trials:</u>	1
<u>Number of Inconclusive Trials:</u>	6
 Total Number of Fish Treated:	 1,698
 Treatment Regimes Used:	
<u>2.2 mg/kg body weight (one injection)</u>	1 trial
<u>6.6 mg/kg body weight (one injection)</u>	6 trials
<u>10.0 mg/kg body weight (one injection)</u>	1 trial
<u>10.0 mg/kg body weight (two injections)</u>	28 trials
 Treatment Water Temperature (°F):	 48.0 - 72.8
 Size of Treated Fish:	 Adult
 Species Treated:	 channel catfish <i>Ictalurus punctatus</i> muskellunge <i>Esox masquinongy</i> northern pike <i>Esox lucius</i>
